CONTROLLING pCO_2 IN HIGH DENSITY PERFUSION CULTURES

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Two important trends in the biopharmaceutical industry over the last 10 years are combining to provide challenges for bioprocess engineers. Firstly, the trend towards high viable cell concentration (VCC) perfusion cultures (>1 x 10^8 mL^{-1}) has increased the mass transfer requirements. Secondly, the trend towards single use bioreactors (SUBs) means that weaker materials are used for the construction of bioreactors limiting the range of conditions that can be employed to meet the mass transfer requirements.

High VCC cultures have two distinct mass transfer requirements. Firstly, transferring in enough oxygen to meet the culture's oxygen demand. Secondly, removing enough carbon dioxide to prevent the partial pressure of carbon dioxide (pCO_2) from accumulating to inhibitory levels. This poster focuses on the causes of pCO_2 accumulation and control strategies to prevent this accumulation.

Under industrial culture conditions the dissolved oxygen concentration in the culture is kept constant. Cells in culture have a respiratory quotient of around 1. An important implication of this is that the pCO_2 level in a culture will only hold steady when the oxygen transfer rate (OTR) into the culture approximately equals the carbon dioxide transfer rate (CTR) out of the culture. If the OTR is increased without increasing the CTR (eg by oxygen enrichment) metabolic carbon dioxide will accumulate in the culture until the pCO_2 is sufficiently high to drive a higher CTR such that CTR = OTR again.

We have characterised the impact of a number of vessel design features and process control handles on the ratio of OTR to CTR for three single use bioreactor systems. From the resulting model it was possible to estimate the pCO_2 of a culture under defined process conditions given a specified oxygen demand. The impacts of vessel design, oxygen enrichment, power dissipation and gas flow rate on pCO_2 will be presented and the implications for pCO_2 control strategies discussed.